

REMARKS

Claims 32-35 are pending and are rejected. Claim 32 is amended to correct spelling. New claims 45-50 recite selected individual members of the Markush group of claim 35 and thus are fully supported and introduce no new matter.

DOUBLE PATENTING REJECTION

Claims 32-34 are rejected for obvious-type double patenting over claim 1 of Achilefu U.S. Patent No. 6,395,257. Applicants attach a Terminal Disclaimer over the '257 patent.

CLAIM REJECTIONS UNDER 35 U.S.C. §103

Claims 32-35 are rejected under 35 U.S.C. §103(a) as obvious over Eversole.

The Examiner states that it would be obvious

...to modify the invention of Eversole et al to encompass the concentration range of biocompatible organic solvent; thus, enhancing fluorescence to the photodiagnostic procedure... Both Applicant and Eversole et al disclose methods which involve compositions comprising a dye and a compatible organic solvent.

The Examiner's reasons are that

...both Applicant and Eversole et al are using a composition comprising the same components (a dye and a biocompatible organic solvent) and Figure 8 of Eversole et al disclose enhanced fluorescence intensity spectra for solutions comprising the acidified and neutralized solutions containing the bromo--cresol green dye-biocompatible organic solvent combination when compared to the solution containing only the dye.

Applicants disagree. They dispute that Eversole would even be considered by a person of ordinary skill in the art of photodiagnostic or phototherapeutic imaging methods, which is what Applicants claim. Such clinical methods are typically performed by a health care professional by administering a dye and imaging a body part of a patient for diagnosis or therapy. Enhancing fluorescence of the image would improve image quality, and thus improve diagnosis or therapy for the patient.

Eversole, as previously analyzed, discloses "Microdroplet Missing Resonance Spectroscopy". It discloses that "fluorescent emission resonances in ethanol droplets could be utilized to determine additive identification and concentration as well as droplet acidity" (Eversole p. 209, Introduction, next to last sentence). It develops a model from which "additional work with bromo-cresol green dye additives shows diagnostic application of the "missing resonance spectroscopy" could provide new experimental information as a droplet concentration or pH sensor."

Thus, Eversole's "diagnostic" application is not a "method of diagnosis or treatment", as Applicants claim. In contrast, Eversole teaches in vitro use, not in a patient, and looks at a dye to obtain a "model of relative emission intensities" that provide information on droplets (Eversole p. 215, Discussion first sentence), whereby "light can be trapped inside droplets by total internal

reflection (p. 209 Abstract) by the mechanism of total internal reflectance at the droplet surface (Droplet Resonances, first paragraph). Eversole produces ethanol droplets, doped with rhodamine-6G dye, by using a vibrating orifice generator. Eversole's end result is to "provide new experimental information as a droplet concentration or pH sensor".

Such data in the physical sciences to provide microdroplet data does not address the issue of enhancing fluorescence when a dye is administered to a patient to image or treat a body part. There is no teaching, motivation, or suggestion to administer Eversole's composition to a patient for a photodiagnostic or phototherapeutic procedure, and a person of ordinary skill in the art of Applicants' claimed method would not look to Eversole. Thus Applicants respectfully dispute the rejection and request its withdrawal.

Claims 32-35 are rejected under 35 U.S.C. §103(a) as obvious over Licha U.S. Patent No. 6,083,485. Applicants respectfully disagree.

The Examiner cites Licha as disclosing its dyes may be added to a n-octanol/Tris buffer (column 9, lines 54-64). The Examiner rejects Applicants' claims as obvious because

while Licha et al do not specifically state that fluorescence is enhanced when the dye is in the presence of the compatible organic solvent, a skilled practitioner in the art would recognize that since both Applicant and Licha et al disclose dyes in combination with a biocompatible organic solvent (i.e., isopropanol), it would be inherent that in both instances fluorescence." [sic]

The Examiner states that because Applicants and Licha disclose the same components, and because a composition is inseparable from its properties, enhanced fluorescence would be exhibited by Licha's composition.

However, a person of ordinary skill in the art knows that adding n-octanol/Tris buffer to any agent is a well known method to provide a hypothetical equilibrium measurement of the agent between n-octanol/water (or aqueous buffer), or membrane/water phases. See each of the following attached references in support: Barton et al. *J. Pharmaceutical Sciences* (1997) 86, 1034; Leo et al. "Partition coefficients and their uses". *Chem Rev* 71 (1971), 6, 525 (see at least ¶ spanning pp. 525-526, ¶ bottom of col. 1 p. 527, ¶ spanning p. 540-541, and ¶ bottom of col. 2 p. 541); and Moriguchi et al. (1992) "Simple method of calculating octanol/water partition coefficient" *Chem Pharm Bull* 40, 1, 127.

Licha does not disclose adding an organic solvent to a dye that is administered to a patient, in contrast, Licha adds an organic solvent pre-administration to a patient, to determine dye equilibrium properties. This does not teach, suggest, or motivate use in a patient to enhance fluorescence, and thus a person of ordinary skill in the art would not look to Licha. Fluorescence enhancement is not required for the process of equilibrium partitioning.

The Examiner cites Licha Examples 2 and 7 as disclosing a dye dissolved in isopropanol. Applicants respectfully assert that, in each of these examples, isopropanol is used in a "purification/isolation" procedure to purify or isolate the compound, as one by a person of ordinary skill in the art. In such schemes, isopropanol is removed and the crystalline purified compound is recovered. Hence, Applicants disagree that Licha teaches, motivates, or suggests a compound's inherent fluorescence properties, if any, are enhanced by the organic solvent. In fact, there is no teaching of an organic solvent present along with the dye that is to be administered. Hence, Applicants assert Licha does not render Applicants' method obvious and respectfully requests the rejection be withdrawn.

CONCLUSION

Applicants believe the application is in complete condition for allowance. The Terminal Disclaimer fee is being paid by credit card (see Electronic Fee Authorization sheet). No other fees are believed due but, if deemed necessary, they are authorized to be charged to Deposit Account No. 20-0809.

Respectfully submitted,

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